REMARKS

I. Non-compliance

The Office Action alleges that the response of January 16, 2007 was non-compliant because the new and amended claims fall outside the elected subject matter. While Applicant respectfully disagrees, the claims have been amended in an effort to conform the subject matter to the elected subject matter of Group I.

II. Claim Status

Claims 1, 2, and 51-60 have been canceled.

Claims 61-69 have been added. No new matter has been introduced. The claims find ample support in original claims 1-12 and throughout the specification. Specifically, claim 61 corresponds to a combination of original claims 1 and 3 (Group I). Claim 62 corresponds to original claim 2 (Group I). Claim 63 corresponds to original claims 6 and 7 (Group I). Claim 64 corresponds to original claim 9 (Group 1). Claim 65 relating to PDZ domains finds ample support in the Description, for example, on page 6, paragraph [0024]. Claim 66 corresponds to original claim 10 (Group I). Claim 67 corresponds to original claim 11. Claim 68 corresponds to original claim 12. Claim 69 relating to RSV finds ample support in the Description on page 8, paragraph [0033] and page 13, paragraph [0052] and throughout.

III. Novelty

Anticipation Standard

In order for a reference to anticipate the invention under 35 U.S.C. § 102, each and every element of the claimed invention must be taught in the reference.

Karrer Reference

Claims 1-3, 5-6, and 8-12 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Karrer (WO 01/32712). Applicant respectfully traverses the rejection because Karrer fails to teach or suggest every element of the claimed invention.

Karrer reports on pages 85-87 coevolution of antibodies and antigens as a means to overcome poor antigenicity of the target antigen. According to the reported method, the parent target antigen has no corresponding neutralizing agent at the outset, so the diversification and selection steps are aimed at developing increased antigenicity to develop a neutralizing antibody where none existed. In contrast, the present invention starts with a target (e.g., an antigen) which is already neutralized by an existing neutralizing agent. Diversification of the target is designed to anticipate and predict the potential for the target to develop a resistance to the existing neutralizing agent. Once resistance is obtained, diversification and selection of neutralizing agents is then carried out to find neutralizing agents that can neutralize the resistant targets. In this way, potential resistances are predicted and agents with the ability to neutralize the anticipated resistances are prepared in advance.

Because Karrer focuses on improving the antigenicity of a target and, thus, the weakening of a target's resistance to potential neutralizing agents, the reference fails to teach a method of countering the development of resistance. Nowhere in the reference is it taught or suggested that in vitro coevolution can be used to predict the development of resistances and to generate new agents that will neutralize the resistant targets. Thus, Karrer fails to teach, *inter alia*, coeveolution of a parent target (e.g, antigen) and a parent neutralizing agent (e.g., antibody) that neutralizes the parent target because Karrer only reports coevolution for non-neutralizing parent antibody/antigen pairs. Further Karrer fails to teach the selecting of one or more next generation targets having improved resistance to the parent neutralizing agent because Karrer does not teach or suggest a method of countering the development of resistance.

Karrer further fails to teach PDZ domains and RSV virus.

Because Karrer fails to teach or suggest all the elements of the claim, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b).

McCafferty reference

Claims 1-3, 5-6, and 9-12 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by McCafferty (US Pat. No. 6,916,605). Applicant respectfully traverses the rejection because McCafferty fails to teach or suggest all the elements of the claimed invention.

Applicant first notes that both the original and amended claims include diversification and selection steps for both the parent target and the parent neutralizing agent, hence, coevolution. McCafferty fails to teach not only a method of countering the development of resistance, but coevolution in general, because McCafferty fails to teach diversification and selection steps for both the parent target and the parent neutralizing agent. Specifically, McCafferty appears to report preparing a genetically diverse population of one member of a binding pair followed by selection from this population. However, McCafferty fails to teach or suggest the diversification and selection of the other member of the binding pair. Each of the places in the reference pointed to in the Office Action as supporting the present rejection fail to identify diversification and selection steps applying to both a parent target and parent neutralizing agent (e.g., both members of a binding pair). Thus, McCafferty fails to teach or suggest all the elements of the claimed invention because, *inter alia*, there is no teaching of the diversification and selection of both parent target and parent neutralizing agent. Accordingly, McCafferty also fails to teach or suggest 1) coevolution, 2) a method of countering the development of resistance, and 3) and the selection of a next generation target having increased resistance.

Because McCafferty fails to teach every element of the claims, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(e).

III. Written Description

Claims will lack adequate written description under 35 U.S.C. § 112, first paragraph, if the specification fails to reasonably convey that the Applicant had possession of the claimed invention at the time the application was filed.

Claims 1-3, 5-6, and 8-12 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicant respectfully traverses the rejection because the specification more than adequately conveys that the Applicant had possession of the invention at the time the application was filed.

The Office Action alleges that the claims are not adequately described because they are 1) too broad (e.g., encompassing any cell, protein, nucleic acid, small molecule, virus, or organism) and 2) lack information about how resistance can develop.

With respect to the first point of overbreadth, Applicant respectfully disagrees because the claims pertain to target-neturalizing agent pairs involving cells, proteins, nucleic acids, small molecules, viruses, and organisms where target resistance can occur. Thus, not all cells, proteins, nucleic acids, small molecules, viruses, and organisms are contemplated by the claim, just those that dynamically interact with another agent in a neutralizing capacity or ability to resist the same.

With respect to the second point of alleged lack of information, knowledge of the specific mechanism by which resistance develops or the specific mutations that occur is not necessary for practicing the invention because the process of diversification and selection is, by its nature, meant to minimize dependence on such knowledge for success. That is, according to the claimed methods, one could develop a newly resistant target without knowledge of why or how it is resistant, and then go on to prepare a neutralizing antibody to the resistant target without knowing why or how the new antibody is neutralizing because the diversification/selection process allows rapid screening of a very large number of targets and neutralizing agents regardless of their mutations. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 90, 94 (Fed. Cir. 1986). Methods of screening large populations of different and unknown mutants to find a particular phenotype are well known in the art as evidenced by the numerous references cited in the specification on pages 15 to 18. Accordingly, the methods of the invention can be carried out without specific structural knowledge of mutations conferring resistance, and thus such information need not be provided for complying with the written description requirement.

The policy behind the written description requirement is to promote the useful arts such that, in exchange for the right to exclude others, the Applicant discloses to the public what it is he/she has invented. The invention is adequately disclosed to the public when one skilled in the art would have reasonably concluded that the Applicant had possession of the claimed invention. Here, the Applicant adequately disclosed the claimed invention to the public because each of the diversifying and selecting steps for an antigen/antibody system is well detailed in the specification in such a way that one skilled in the art would readily understand that Applicant had possession of the invention at the time of filing. Example 1 more than adequately shows that

the Applicant had possession of the invention because it clearly illustrates, for at least an antigen/antibody system, how one would carry out each of the steps of the claimed methods. Example 1 details how one skilled in the art could carry out the diversifying and selecting steps to find a resistant antigen target (RSV MARMS) and the diversifying and selecting steps to prepare a monoclonal antibody that neutralizes the resistant target. Further description of diversification and selection techniques are provided in the Description on pages 15 to 18. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

IV. Restriction Requirement

Applicant would like to respectfully note that the statement in the Office Action on page 3, paragraph 4, that the "election of both 'countering the development of resistance in a parent target to a parent neutralizing agent' as a species of what the method is for and 'desired neutralization profile' as the species of the outcome are contradictory" is incorrect. Because the claimed methods prepare a resistant target followed by a neutralizing agent that has increased neutralizing activity against the resistant target (e.g., a desired neutralization profile), both elections of "countering the development of resistance" and a "desired neutralization profile" can readily coexist and are not contradictory.

Applicant further objects to the treatment of the restriction requirement as being made without traverse. Applicant believes that the reasons for traversal already of record are more than adequate to support a traversal.

V. Claim Objections

Applicant respectfully disagrees with the statement on page 4, paragraph 7, that one of skill in the art would assume that all of the coevolved parent targets and parent neutralizing agents would not result in the countering of the development of resistance because of an alleged lack of nexus between the preamble and the last step of the method. One of skill in the art would readily understand how the steps of the invention would lead to the countering of resistance because the countering of resistance naturally flows from the recited steps. However, Applicant

has amended the claims to provide the allegedly requisite nexus. Accordingly, Applicant respectfully requests withdrawal of the objections to the claims.

VI. Conclusion/Request for Extension

Applicant believes the claims as amended are in condition for allowance and respectfully requests the same.

Applicant hereby requests a one-month extension of time for reply. Applicable extension fees are provided herewith.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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